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EDITORIAL COMMENT

Radial Access for Primary Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction

Time for a Paradigm Shift?*

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In the past 2 decades there has been tremendous evolution of both the effectiveness and safety of percutaneous coronary intervention (PCI). As coronary ischemic events have decreased dramatically in frequency during and after PCI, efforts to improve the safety of PCI have shifted to addressing other complications, especially bleeding, occurring in the periprocedural period. A growing body of literature has shown that periprocedural bleeding is an independent predictor of adverse events including death following PCI (1). The term "bleeding avoidance strategies" has emerged reflecting that multiple factors have been associated with an increase in bleeding, and may have additive effects on this outcome (2). Although multiple factors contribute to bleeding after PCI, the access site (i.e., femoral or radial artery) has recently come under intense scrutiny as a source of potential bleeding, and by extension, a potential modifiable factor in an effort to reduce bleeding complications.

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The safety and efficacy of cardiac catheterization (CATH) and PCI performed via the radial (RA) or femoral access (FA) in a wide variety of patients and circumstances has been assessed in a number of small randomized trials and multiple registries. In a recent meta-analysis of PCI studies performed from both RA and FA incorporating many of these studies, RA was found to have better outcomes compared to FA for all metrics evaluated including access site complications, bleeding, and death (3). Recently, the RIVAL (RadIal Vs. femorAL) trial evaluated 7,021 patients with an acute coronary syndrome randomized to undergo PCI from either RA or FA (4). A significant reduction in the rates of major vascular access complications from 3.7% to 1.4% with the use of RA compared with FA was observed but no substantial differences in overall rates of bleeding or in mortality were found. Based on the results of these studies, and educational initiatives highlighting the relative safety of the radial approach, there has been an upsurge in the utilization of RA for both CATH and PCI (5).

As interest in utilization of RA for elective PCI has grown, there has also been an increasing interest in the use of RA for primary percutaneous coronary intervention (PPCI) for ST-segment elevation myocardial infarction (STEMI). Although there was not a significant reduction in the primary endpoint in the overall RIVAL cohort, in the subgroup of patients treated with PPCI for STEMI (approximately one-third of the overall cohort), there was a significant reduction in the primary endpoint with RA compared with FA, including a decrease in mortality. In the RIFLE-STEACS (Radial Versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome) trial comparing outcomes in STEMI patients randomized to either RA or FA, similar observations were made (6). Interestingly, in the subgroup of STEMI patients in the RIVAL trial as well as in the MORTAL (Mortality benefit Of Reduced Transfusion after percutaneous intervention via Arm or Leg) trial (7) and the RIFLE-STEAC trial, there was a significant reduction in mortality with the radial approach as opposed to the femoral approach. Although these studies were not designed to address mortality as the primary endpoint, nor the potential mechanism of lower mortality with RA, it is presumed that the decrease in mortality observed with RA was related to a decrease in access site and bleeding complications associated with the radial approach.

In this issue of the *Journal*, 2 studies further address the issue of RA versus FA for PPCI for STEMI. First, Bernat et al. (8) present the results of the STEMI-RADIAL trial (ST Elevation Myocardial Infarction Treated by RADIAL or Femoral Approach), a multicenter (n = 4) randomized trial of PPCI for STEMI. The study was designed to evaluate only PPCI for STEMI, and excluded patients with thrombolysis or cardiogenic shock who were included in the STEMI subgroup of RIVAL and in RIFLE-STEACS. The primary endpoint was the cumulative incidence of major bleeding and access site complications at 30 days, with a second primary endpoint of net adverse clinical events (NACE) defined as a composite of death, myocardial infarction, stroke, and major bleeding/vascular complications. The primary endpoint occurred in 1.4% of RA (n = 348) and 7.2% of FA (n = 359; p = 0.001). NACE occurred in 4.6% of RA and 11.0% of FA (p = 0.028), although mortality rates were similar (2.3% vs. 3.6%, respectively; p = 0.31). The authors concluded that "in patients with STEMI undergoing PPCI by operators

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experienced in both access sites, the radial approach was associated with significantly lower incidence of major bleeding and access site complications and superior net clinical benefit. These findings support the use of the radial approach in PPCI as first choice after proper training."

In the second study, Jolly et al. (9) evaluated the role of center and operator RA and FA volume on procedural metrics and clinical outcomes in a substudy of the RIVAL trial. The authors found a strong interaction between overall and RA center volumes, and clinical outcomes, but not FA center volumes. Overall PCI and RA operator volumes were also associated with lower rates of the primary study endpoint. The rationale offered by the authors of this apparent dichotomy was that femoral volumes were much higher than reported in previous studies such that all centers were equally expert in femoral, but not radial, PCI. As the impetus to increase utilization of RA increases, the issue of RA experience will become important in the overall discussion of the relative merits of RA versus FA for PCI. What constitutes proficiency sufficient to be characterized as "radial expert" remains unclear. Experience as little as 50 cases has been suggested as the minimum to develop proficiency (10), but multiple studies indicate that continued proficiency continues to be accrued with higher RA volumes, particularly at high- volume radial centers.

The results of the RADIAL-STEMI trial (8) and the RIVAL substudy (9) complement the observations made from the STEMI subgroup of RIVAL (4) and RIFLE-STEACS (6) trials. Each of the studies used slightly different endpoints so it is difficult to precisely compare results, but some reasonable generalizations can be made about these studies. The reduction in access site complications with RA compared with FA was directionally similar in all studies. Interestingly, overall bleeding was not reduced in these studies, largely because non–access site bleeding was not different for the RA and FA groups, and accounted for at least 50% of overall major bleeding. Mortality was lower in the RA versus FA groups in the STEMI subgroup of RIVAL and in RIFLE-STEACS trials, but not in the RADIAL-STEMI trial. As the authors of the RADIAL-STEMI trial concluded, the results from these studies make a strong argument for considering a paradigm shift to RA rather than FA for PPCI of STEMI.

The issue of a potential decrease in mortality with RA versus FA in PPCI for STEMI is important as it would provide a compelling argument to switch to a preferred RA approach, rather than switching based on a reduction in access site complications alone. In the August issue of *JACC: Cardiovascular Interventions*, Karrowni et al. (11) presented a meta-analysis of RA versus FA trials (n = 12) of PPCI for STEMI and found an odds ratio of 0.55 (95% confidence interval [CI]: 0.40 to 0.76; $p < 0.001$) for a decreased risk of death with RA versus FA. In an accompanying editorial Mahmud and Patel cautioned against overinterpretation of these observations because of methodologic differences in the studies, and urged for an adequately powered clinical trial to provide a definitive answer to the issue of a reduction in mortality with RA for PPCI for STEMI (12). Nonetheless, in the absence of a definitive answer to the question of a reduction in mortality with RA, the existing data suggest that at worst RA is equivalent to FA with regard to mortality, and may well be lower.

The RA approach was introduced several decades ago but received little uptake because of issues including spasm, variations in the pathway from the wrist to the ascending aorta, limitations in catheter sizes, as well as less than optimal equipment tailored specifically for the radial approach (13). However, improvements in technology, and in technique, have dramatically overcome many of these limitations. Yet several concerns persist among interventionalists, particularly with regard to PCI performed from the RA, that continue to limit wider utilization of this approach, including: concern that RA takes longer and is associated with higher radiation exposure than FA cases; the RA will make adherence to a 90-min door-to-balloon time (DTB) metric problematic; and that it may limit interventional options in complex cases.

The perception that RA has a "steep learning curve," takes longer to perform, and is associated with higher radiation exposure have been addressed by multiple studies as well as by a post hoc analysis of the RIVAL trial (14). In the RIVAL trial, overall fluoroscopy times were slightly longer for radial than femoral—9.3 min (95% CI: 5.8 to 15.0 min) versus 8.0 min (95% CI: 4.5 to 13.0 min; $p < 0.01$)—but these differences were substantially mitigated by high-volume operators and centers. Similarly, air kerma was slightly higher for radial compared with femoral cases, but the difference was seen almost exclusively among low-volume centers. These data, as well as the data from Bernat et al. (8) strongly support the concept that experience with RA can eliminate differences in procedure time and radiation exposure between these two approaches, while preserving the safety benefit of RA versus FA.

Despite a widely held perception in the United States that radial PPCI for STEMI takes "a lot longer" and FA is the preferred approach, the existing data suggest that the increase in time associated with the radial approach is small and does not preclude performing routine STEMI cases with a DTB time under 90 min (15,16). In the RIFLE-STEACS trial DTBs were 53 min (31 to 91 min) for radial and 60 min (35 to 99 min) for femoral ($p = 0.175$) (6). Thus, there was a small nonsignificant increase in DTB with the radial approach, but DTBs well under 90 min were still achieved with the radial approach. In the RADIAL-STEMI trial, DTBs were very low and similar in both RA and FA groups, 32 ± 11 min and 31 ± 11 min, respectively ($p = 0.31$). Crossover rates for RA, necessitating a femoral approach anyway, are a particular concern in PPCI for STEMI. However, the crossover rate for RA to FA in the RADIAL-STEMI trial was only 3.7% and the analysis of DTB was done on an intention- to- treat basis. Admittedly, the radial operators in both studies were very experienced, but these

consistent observations should dispel the notion that PPCI cannot be performed in a timely fashion from the radial approach with adequate training and experience. As noted in their editorial, Mahmud and Patel caution that PPCI for STEMI should only be attempted when substantial experience with RA in elective cases has been obtained (12).

There also has been concern among interventionalists that the radial approach may limit their options in complex cases, and that the urgent need for revascularization in a STEMI case requires the most flexible approach be taken (i.e., FA). However, techniques have evolved that allow complex PCI, for example use of a sheathless guide technique, and sequential two- stent strategies among others, as well as treatment of graft patients via the left radial artery. Finally, patients with shock complicating a STEMI are problematic. If support devices are expected to be required, a FA approach is needed for the support device, with PPCI performed from RA or FA on the basis of the operators' experience and comfort level. Ultimately, these technical considerations do not appear to be issues among high-volume RA operators at high- volume centers.

The studies reviewed above are helping shape the evidence base surrounding the relative benefits of RA versus FA for PPCI for STEMI. What should we take away from these studies? First, in experienced centers with experienced operators, procedures performed from the radial artery can be performed in the same length of time, using the same amount of radiation and contrast, as the same procedures performed from the femoral artery. Second, access site complications are consistently lower with RA than FA, as would be expected. Third, PPCI for STEMI can be performed via RA with DTBs clinically equivalent to those performed from FA after adequate experience and training. Finally, mortality is the same or possibly lower with RA versus FA for PPCI for STEMI. Based on these considerations is it time for a paradigm shift to a preferred RA approach for PPCI for STEMI? Based on these new studies the answer appears to be yes. Moreover, this transition from preferred FA to preferred RA for PPCI for STEMI represents a natural evolution of strategies aimed at improving safety of coronary interventions. To reap the full benefit of the radial approach, however, a concerted effort by both interventional centers and operators to achieve proficiency in performing PCI from the radial artery will be needed.

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